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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,402	09/17/2001	Julio Cesar Aguilar Rubido	976-11 PCT/US	3056

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EXAMINER	
SALVOZA, M FRANCO G	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 01/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/857,402	AGUILAR RUBIDO ET AL.	
	Examiner	Art Unit	
	M. Franco Salvoza	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-18,21-23,25-27 and 38-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-18, 21-23, 25-27 and 38-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 15-18, 21-23, 25-27 and 38-42 are currently pending.

Claim Rejections - 35 USC § 102

MAINTAINED

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 15, 16 and 21-23 were rejected under 102(b) for being anticipated by Tabor et al. in light of Bowen et al.

Applicant argues that the claims are restricted to vaccine formulations suitable for mucosal administration containing HBsAg antigen and a second vaccine antigen which is a viral nucleocapsid or a virus-like particle, and there is no disclosure or suggestion in the cited references of a formulation for mucosal administration having HBsAg antigen and a viral nucleocapsid or a virus-like particle.

Applicants arguments are considered but found unpersuasive. Tabor et al. teaches a combination vaccine formulation comprising a mixture of 20 μg of HBsAg and 50 μg of Hepatitis B nucleocapsid. In response to applicant's argument that the references do not teach a vaccine composition suitable for mucosal administration, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior

art structure is capable of performing the intended use, then it meets the claim. The rejection is maintained for reasons of record.

Claim Rejections - 35 USC § 103

MAINTAINED

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17, 25, 27 and 38-41 were rejected under 35 U.S.C. 103(a) as being unpatentable over Tabor et al. in light of Bowen et al., and further in view of Rose et al., and Hauser et al. Claims 15, 18 and 26 were rejected under 103(a) as being obvious over Wands et al.

Applicant argues that in addition to the teachings of Tabor et al. Bowen et al. as recited above, Rose et. al discloses the administration of HPV VLPs; Hauser et al. discloses vaccine compositions that are administered intramuscularly; Wands et al. discloses fusion proteins containing HBsAg and HCV core proteins. Applicant argues that the claimed invention is not obvious.

Applicants arguments are considered but found unpersuasive. In response to applicant's argument that the references do not teach a vaccine composition suitable for mucosal administration, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the

claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The rejection is maintained for reasons of record.

Claim Rejections

NEW

Applicant pointed out that claim 42 was not rejected over any prior art references in the previous action. The Office kindly thanks applicant for bringing this to the Office's attention. The omission was inadvertent, and the proper rejection follows.

Claim Rejections - 35 USC § 112

NEW

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17, 18, 25, 26, 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for vaccine formulations suitable for mucosal administration to elicit enhanced antibody response, does not reasonably provide enablement for suitability of preventative or therapeutic vaccines against HPV and therapeutic vaccines against HCV. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for

enablement under 35 U.S.C. 1 12 ! 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988) and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

As indicated above, claims 17, 18, 22, 25, 26 and 27 broadly recite vaccine compositions suitable for use as a preventative and therapeutic vaccine against HPV and a vaccine composition suitable for use as a therapeutic vaccine against HCV infection.

References reviewing the state of the art for these particular diseases indicate that, while progress is being made, prospects for therapeutic vaccines for HCV and HPV and a preventative vaccine against HPV are still in the early stages and unpredictable. For example, Houghton et al. ("Prospects for a vaccine against the hepatitis C virus," *Nature*, Vol 436, August 18, 2005) underscores the difficulty in finding successful therapeutic vaccine options for HCV: "many therapeutic vaccines trials are planned or are already in progress and use delivery methods and formulations but little information is available about their efficacy at present." (p. 964). Additionally, the current standard of care for such therapy involves the use of IFN-α and ribavirin, which only results in sustained viral response in only 50% or less of patients (p. 964). In regards to HPV, Roden et al. ("Preventative and therapeutic vaccines for cervical cancer," *Expert Rev. of Vaccines*, 2(4); 496-516 (Aug. 2003) states that HPV preventative vaccines even

have yet to be tested in patients while research still is needed for therapeutic vaccines, citing HPV E6 and E7 merely as possible targets for promising research for controlling infection and lesions (p. 508).

Applicant's disclosure does contain examples of mucosal administration of HBsAg in mice, citing enhanced antibody response with the coadministration of HBsAg with HBcAg as well as HPV VLP and HCV nucleocapsid through statistical analysis. However, the disclosure does not sufficiently teach enough beyond that to counter the teachings in the art. Raising antibodies and raising antibodies in higher levels does not necessarily confer protection or successful treatment against these diseases. Surely a mere increase in antibody titers does not rise to the level of a broad claim for suitability for use as a preventative or therapeutic vaccine against these diseases.

In view of the breadth of the claims, the lack of examples or guidance, and the fact that those in the art would not be able to determine without extensive experimentation how to use the vaccine compositions therapeutically or in a preventative manner against HCV and HPV beyond eliciting antibodies, the application has not provided sufficient information to enable those in the art to practice the claimed invention without undue experimentation.

Claim Rejections - 35 USC § 103

NEW

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 42 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tabor et. al in view of McCluskie et al. ("Immunization Against Hepatitis B Virus by Mucosal Administration of Antigen-Antibody Complexes," *Viral Immunology*, Vol. 11, No. 4, 1998, pp. 245-252).

Claim 42 recites a method for administering a vaccine formulation to a mammal for generating an immune response, the method comprising administering mucosally to the mammal a vaccine formulation comprising: a mixture of a first vaccine antigen which is Hepatitis B virus surface antigen (HBsAg) and a second vaccine antigen which is a viral nucleocapsid or a virus-like particle; wherein said HBsAg has an adjuvant effect on the second vaccine antigen, and wherein said first and second vaccine antigen are each present from 0.001 mg to 1 mg.

Tabor et al. teaches a vaccine formulation comprising a mixture of HBsAg and hepatitis B nucleocapsid administered subcutaneously. Tabor et al. does not teach mucosal administration of the vaccine formulation.

McCluskie et al. teaches mucosal administration of a vaccine formulation to mice comprising HBsAg complexed with antibodies against HBsAg for generating an immune response. (p. 245)

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the vaccine composition of Tabor et al. and the mucosal administration method of McCluskie et al. because McCluskie et al. teaches that mucosal administration of complexed HBsAg can induce a substantial immune response. "Administration of a vaccine to a mucosal surface can induce both systemic and mucosal immune responses, whereas parenteral administration will usually induce only systemic immunity" (p. 246). Furthermore, McCluskie et

al. adds as further motivation for Hepatitis B vaccine mucosal delivery the facilitation of mass vaccination programs if HBV vaccines could be administered via a noninvasive route, the lack of need for highly trained personnel, and the elimination of risk of needle-stick injury or cross contamination (p. 246).

One of ordinary skill in the art at time the invention was made would have had a reasonable expectation of success for using the vaccine composition of Tabor et al. with the method of mucosal administration of McCluskie et al. because Tabor et al. and McCluskie et al. both teach administration of HBsAg vaccine compositions to elicit immune responses against Hepatitis B.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to M. Franco Salvoza whose telephone number is (571) 272-8410. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

M. Franco Salvoza
Patent Examiner

JAMES HOUSEL 12/24/05
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